

# Structural studies of porins from *Campylobacter jejuni* and *Enterobacter aerogenes*

## ABSTRACT

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The increasing of multidrug resistance (MDR) amongst bacteria is a global concern for public health. MDR is most serious in Gram negative bacteria due to their additional outer membrane, whose low permeability makes the influx of antibiotics more difficult. Embedded in the outer membrane, water filled channels, known as porins, represent a “gate” through which small hydrophilic molecules such as sugar, drugs and chemicals can enter the cell (1). As a resistance mechanism, porins can be down-regulated and/or mutated when bacteria are pressured by antibiotics (2). Thus, a better understanding of porins structure will help us to clarify how they interact with antibiotics and hence accelerate the design of new drugs. Here we present the structural studies we performed on MOMP and Omp50 from the pathogenic *Campylobacter jejuni* and omp 35, omp36 and omp37 from the pathogenic *Enterobacter aerogenes*. MOMP, purified from the native *C. jejuni*, was solved at 2.89Å resolution. The structure shows that MOMP is a trimeric 18-stranded porin with the typical β-barrel character and identifies a bound metal ion at the constriction zone, which molecular dynamics revealed to be important for stability and antibiotics translocation. Omp50 was overexpressed and purified in *E. coli* and crystals trials have been already started. Omp35, Omp36 and Omp37, expressed and purified in *E. coli*, were successfully crystallized. Structures were solved at 2.8, 2.4 and 2.7Å, respectively. The structures show that Omp35, Omp36 and Omp37 are trimeric 16-stranded porin with the typical β-barrel character. Liposome

swelling assay was performed to test permeation of a choice of antibiotics used to treat *E. aerogenes* infections.

#### References

- (1) S. Galdiero, A. Falanga, M. Cantisani, R. Tarallo, M.E Della Pepa, V. D'Orlando, M. Galdiero. Microbe-Host Interactions: Structure and Role of Gram-Negative Bacterial Porins. *Current Protein and Peptide Science*. **2012**, 13,843-854.
- (2) Lavigne, JP; Sotto, A; Nicolas-Chanoine, MH; Bouziges, N; Pagès, JM; Davin-Regli, A. An adaptive response of **Enterobacter aerogenes** to imipenem: regulation of porin balance in clinical isolates. *Int J Antimicrob Agents*. **2013** ;41(2):130-6 .